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PATENT SPECIFICATION

DRAWINGS ATTACHED

888,038

Date of Application and filing Complete Specification: Dec. 16, 1959.

No. 2 23/59.

Complete Specification Published: Jan. 24, 1962.

Index at acceptance:—Class 81(1), B2(L: N: P: S: T), B(3: 6).

International Classification:—A61k.

COMPLETE SPECIFICATION

Medicinal Tablet

I, WILLIAM WARREN TRIGGS, C.B.E., a British subject, of Messrs. Marks & Clerk, 57 & 58, Lincoln's Inn Fields, London, W.C.2, do hereby declare the invention (Communicated by The Wander Company, a United States Company, of Prudential Plaza, Chicago 1, Illinois, United States of America) for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement: —

This invention relates to a novel and improved medicinal tablet and more particularly to a tablet other than an implantation tablet containing substantially segregate quantities of the same or different ingredients. The formulation of an implantation tablet would normally be quite different from, for instance, a tablet for oral administration, and this specification does not relate to an implantation tablet.

It is frequently desired to provide medicinal or pharmaceutical compositions in solid, dosage-unit form wherein each dosage unit contains segregated quantities of the ingredients of the preparation. For example, one type of medicinal tablet or pill which is useful for delayed action or multiple dosage medication is the so-called tablet-within-a-tablet or "double tablet" construction which consists of an innermost core tablet, a thin enteric coating around the core tablet, and an outermost shell or layer. Upon oral administration, the medicinal ingredients in the outermost shell are readily assimilated in the gastro-intestinal tract to provide immediate therapy. After a predetermined period of time, the gastrointestinal fluids dissolve the enteric coating on the inner core portion of the tablet and the ingredients of the latter are then available for assimilation. Thus, a sustained or delayed action effect is realized which is equivalent to the result which would be obtained by repeated administration of conventional tablets over a period of time. Another type of medicinal tablet which is also employed in certain instances is the so-called layered tablet which consists of two or more superimposed layers of medicinal ingredients compressed together to form a unitary tablet. A layered or multiple compressed tablet of this type is used primarily in situations where it is necessary to separate or segregate two different pharmaceutical ingredients which are to be administered at the same time but which have an adverse effect upon each other so that they cannot be intimately comingled beforehand. For example, an acidic medicinal ingredient may have a detrimental effect on a companion ingredient which is succeptible to acid action.

However, both the tablet-within-tablet and the layered tablet constructions have serious limitations. For example, in the tablet-within-tablet the inherent geometry of the construction is such that the quantity of medicinal ingredient or ingredients forming the outer shell of the tablet is always substantially greater than the quantity of material forming the inner core of the tablet. In a typical instance, the dosage content in the outer shell may be as much as twice as great as the dosage content of the inner core tablet. Moreover, in the tablet-within-a-tablet construction it is necessarily the outer shell portion of the tablet which is first released and assimilated in the gastroinestinal tract. It will readily be understood that these limitations may frequently restrict the scope and utility of this tablet form.

In the layered tablet, the chief disadvantages are as undesirable merging of the ingredient at the interface between the layers and also a poor degree of control over the relative quantities of the ingredients in the respective layers. These disadvantages are occasioned by the necessity of producing a layered tablet in a single compression step so as to obtain a unitary tablet having the required mechanical strength and coherence. Generally speaking, the layered tablet is formed by successively introducing into a die cavity measured amounts of the respective

[*Price 4s. 6d.*]

Price 25p

granulated ingredients so as to form two or more superimposed layers of the several ingredients. After the die cavity is filled, a plunger compresses the layered granulations in a single operation. Because of the manner in which the granulations are fed sequentially into the die cavity, it is possible to have undesirable and unavoidable variation in the relative amounts of the two layers thereby precluding any high degrees of accuracy in the proportioning of the ingredients. Moreover, the single compression operation results in unavoidable merging of the two granulations or layers at the interface therebetween. As a result, positive and complete separation of two incompatible ingredients can never be realized in a layered tablet construction. It may be pointed out that the tablet-within-a-tablet construction avoids this latter difficulty because the inner core portion is preformed in a first tabletting or compression operation and thereafter the outer shell is compressed around the preformed core so that there is no merging under pressure of the separate granulations.

A primary object of the invention is to provide a novel and improved form of medicinal tablet other than an implantation tablet of the type adapted to contain substantially segregated quantities of ingredients.

Another object of the invention is to provide a novel and improved medicinal tablet other than an implantation tablet which is particularly suitable for containing incompatible ingredients which must be protected from each other.

An additional object of the invention is to provide a novel and improved medicinal tablet other than an implantation tablet which is also especially suitable for delayed action or multiple dosage medication.

Still another object of the invention is to provide a novel medicinal tablet other than an inplantation tablet which ensures positive separation between segregated quantities of ingredients, permits a high degree of accuracy in the relative quantities of ingredients, and is well adapted for production or modern high speed tabletting equipment.

This invention consists in a medicinal tablet other than an implantation tablet, comprising a main body portion with a rcess in at least one side thereof, and an inlay portion disposed in and substantially filling said recess and forming, with said main body portion, a unitary tablet.

In the medicinal tablet according to this invention, at least one of said portions may have coating means associated therewith for retarding assimilation of said portion in the gastrointestinal tract. For instance, the granules of said portion may be coated prior to compression in order to retard the assimilation.

The medicinal tablet of this invention may comprise a main body portion having a pair of recesses in oppositely disposed sides thereof, and an inlay portion disposed in and substantially filling each of said recesses and forming, with the main body portion, a unitary tablet.

In the medicinal tablet, each of said recesses or said recess may be undercut to an extent sufficient to afford mechanical anchorage of the inlay portion.

The invention will be described, by way of example, with reference to the accompanying drawing, of which: —

Fig. 1 is a plan view of a medicinal tablet which is not an implantation tablet;

Fig. 2 is an edge view of the tablet shown in Fig. 1;

Fig. 3 is a transverse section view as seen along the line 3—3 of Fig 1;

Fig. 4 is a view similar to Fig. 3 but showing a modified form of the invention;

Fig. 5 is a sectional view similar to Fig 3 but showing another embodiment of the invention; and

Fig. 6 is a sectional view of still another embodiment of the invention.

Referring first to Figs. 1 to 3 and 5, a medicinal tablet 10 is shown of a conventional overall configuration and having a main body portion 11 with an outwardly opening cavity or recess 12 in one side thereof and an inlay portion 13 contained in the cavity 12 so as to form a unitary tablet construction with the main body 11. A modification is shown in Fig. 5 wherein the main body portion 11 extends radially inwardly to a slight extent around the marginal edge of the opening of the cavity 12 in the side of the tablet so as to provide an overlying peripheral lip portion 14 for retaining and mechanically interlocking with the inlay tablet portion 13. In manufacturing the tablet, the inlay portion 13 is first compressed in a tabletting machine in the usual manner to provide a compressed preform. This preform is then subjected to a further tabletting operation of a conventional character wherein another granulation is compressed around the preform 13 to provide the surrounding body portion 11.

Inasmuch as both the inlay portion 13 and the main body portion 11 of the tablet are formed by independent compression or tabletting steps, it will be understood that highly accurate control can be exercised over the quantities of ingredients which form the two parts of the tablet. Furthermore, since both the inlay portion 13 and the main body portion 11 have exposed outer surfaces, it can readily be arranged to permit either the portion 11 or the portion 13 to be relased first in the gastrointestinal tract with any desired degree of time delay in the release or assimilation of the other portion of the tablet. In the present embodiment as seen in Fig. 3, differential releasability between the portions 11 and 13

of the tablet is realized by using a coated granulation for one portion and an uncoated granulation for the other portion of the tablet. For example, assuming that the inlay portion 13 comprising the smaller dosage of ingredients is to be assimilated first, the portion 13 may be preformed from an uncoated granulation so that this portion is immediately dissolved in the gastric fluids. However, the main body portion 11 of the tablet comprising a larger dosage of the same ingredients may be formulated as coated granulation in which each granular particle has a time delay or enteric coating designed to resist assimilation in the gastric fluids. Such coated granulations are well known in the art and require no detailed description. It will also be understood that the same technique of coated and uncoated granulations or the inlay and main body portions of the tablet may be utilized where the tablet portions contain different medicinal ingredients which have an adverse effect on each other and must, therefore, be protected from each other. Also, it will be appreciated that the larger portion 11 may be formed first and the smaller inlay portion 13 may be formed from a coated granulation for delayed assimilation thereof.

In Fig. 4, a modification of the invention is shown wherein segregation of the inlay and main body portions of the tablet, for purposes of time delay or positive separation of incompatible ingredients, is realized without the necessity of employing a coated granulation for one of the tablet portions. Thus, the preformed inlay portion of the tablet, designated at 16, may be formulated from an uncoated granulation and is then surrounded by a thin enteric coating or envelope 17 of a conventional character. The main body portion is designated at 18 and may also consist of an uncoated granulation which is compressed around the enteric coated inlay portion 16—17. In this modification of the invention the main body portion 18 of the tablet is first released and assimilated in the gastric fluids while the enteric coating 17 protects the inlay portion 16 for a predetermined period of time so as to provide time delayed or sustained medication.

Of course, in addition to the provision of a separate enteric coating or envelope for the inlay portion of the tablet as illustrated in Fig. 4, the particles of the granulation in either or both portions of the tablet may be coated to any desired degree so as to provide a further degree of control over the time release feature and positive segregation feature of the tablet construction.

Various enteric coating materials are well known to those skilled in the art and extended discussion thereof is, therefore, unnecessary. For example, the more common enteric coating materials include cellulose acetate phthalate, tolu balsam, carnauba wax, alcoholic shellac solutions and hydrogenated fats. It will be understood that the same general types of enteric coating materials may be used for coating either an entire compressed tablet portion or the individual particles of a granulation prior to compression.

In Fig. 6, a further modification of the invention is shown comprising a tablet having a main body portion and two separate inlay portions at opposite sides of the tablet. Thus, the two oppositely disposed inlay portions are designated at 19 and 21 with the main body portion being designated at 22. It will be noted that the inlay portions 19 and 21 have exposed surfaces at opposite sides of the tablet and that the material comprising the main body portion 22 extends around the peripheral edges of the inlay portions and is also disposed as a thin layer between the inlay portions so that the latter are completely segregated from each other. As will readily be understood, the previously discussed advantages of the invention are extended even further by means of the double inlay arrangement. For example, the inlay portions 19 and 21 may comprise the same or different pharmaceutical compositions and they may be coated or uncoated so as to provide any desired sequence of delayed or concurrent release between the respective portions 19, 21, and 22 of the tablet in accordance with the means heretofore described.

Merely by way of illustration, the following specific examples represent typical inlay tablets which may be made in accordance with the present invention.

Example I

An appetite depressant tablet is formulated in the manner shown in Figs. 1—3. In the outer layer the particles of the granulation are enteric coated to provide slow release over a period of ten to twelve hours. The inlay portion is formed from an uncoated readily disintegratable granulation for immediate therapeutic effectiveness.

The formula for the outer layer is as follows:

d-amphetamine sulfate	10 mg.
amorbarbital	30 mg.
excipients	q.s.
enteric coating solution for coating granulation	q.s.

The formula for the inlay portion is as follows:

d-amphetamide sulfate	5 mg.
amobarbital	15 mg.
excipients	q.s.
standard granulating solution	q.s.

EXAMPLE II

An oral decongestant tablet is formulated as in Example I with the outer layer comprising a coated granulation and the inlay portion an uncoated granulation.

The formula for the outer layer is as follows:

phenylpropanolamine hydrochloride	50 mg.
pyrilamine maleate	25 mg.
pheniramine maleate	25 mg.
excipients	q.s.
enteric coating solution for coating granulation	q.s.

The formula for the inlay portion is as follows:

phenylpropanolamine hydrochloride	25 mg.
pyrilamine maleate	12.5 mg.
pheniramine maleate	12.5 mg.
excipients	q.s.
standard granulating solution	q.s.

EXAMPLE III

A hypnotic tablet is made in the manner shown in Fig. 4 with uncoated granulations for both tablet portions but with an enteric coating or envelpoe around the inlay portion. Thus, the outer layer is promptly disintegratable for immediate hypnotic effect and the inlay portion begins to disintegrate after three to four hours to maintain or continue the desired effect.

The formula for the outer layer is as follows:

pentobarbital	60 mg.
mephenesin	300 mg.
excipients	q.s.
standard granulating solution	q.s.

The formula for the inlay portion is as follows:

pentobarbital	30 mg.
mephenesin	125 mg.
excipients	q.s.
pharmaceutical glaze shellac granulating solution	q.s.
enteric coating materials for coating inlay portion of tablet	q.s.

Although in the illustrated embodiments the invention has been described in connection with tablets having the conventional round shape, it is to be understood that the features of the invention may also be utilized in tablets of different and less conventional shape such as triangular, rectangular, or cylindrical shaped tablets.

It will be seen that the invention provides a novel tablet construction which affords wide flexibility in the compositing of segregated quantities of medicinal ingredients either for purposes of time delayed medication or protection of incompatible ingredients from each other. At the same time, the tablet form permits of positive separation of the segregated areas with accurate control over the relative amounts of the several portions of the tablet. The final tablet is readily adapted for varying relative dosages of different ingredients and varying orders of releasability depending upon the terapeutic effects desired. Moreover, in most cases conventional tabletting and compression coating machines will require only relatively modifications to adapt them to the production of inlay tablets as herein described, particularly with respect to Figs. 1—4. Finally, the inlay construction of the tablet affords a unique and distinctive appearance, particularly if the inlay portion of the tablet is of a contrasting color with respect to the surrounding body portion thereby contributing significant advantages to the tablet construction both during production and merchandising. For example, during production the presence of an exposed inlay portion of contrasting color with the remainder of the tablets provide instant visual proof that a complete tablet has been made and thereby greatly facilitates inspection of the final product before packaging and shipping.

WHAT I CLAIM IS:—

1. A medicinal tablet other than an implantation tablet, comprising a main body portion with a recess in at least one side thereof, and an inlay portion disposed in and substantially filling said recess and forming, with said main body portion, a unitary tablet.

2. A medicinal tablet according to claim 1 comprising a main body portion having a pair of recesses in oppositely disposed sides thereof, and an inlay portion disposed in and substantially filling each of said recesses and forming, with said main body portion, a unitary tablet.

3. A medicinal tablet acording to either claim 1 or claim 2 in which each of said recesses or said recess is undercut to an extent sufficient to afford mechanical anchorage of said inlay portion.

4. A medicinal tablet according to claim 1 comprising a preformed compressed inlay portion, and an outer layer compressed around and enclosing a major part of said inlay portion but leaving a surface of the inlay portion exposed.

5. A medicinal tablet according to any of the preceding claims in which at least one of said portions has coating means associated therewith for retarding assimilation of said portion thereof in the gastrointestinal tract.

6. A medicinal tablet according to claim 5 in which one of said portions comprises a compressed uncoated granulation readily assimilatable in the gastric fluids and the other

of said portions comprises a compressed coated granulation which is more resistant to assimilation in the gastric fluids.

7. A medicinal tablet according to claim 5 having an enteric coating surrounding said inlay portion, both portions of the tablet having exposed outer surfaces but the coating around said inlay portion retarding assimilation thereof in the gastric fluids.

8. A medicinal tablet according to any of the preceding claims which has been formulated for oral administration.

9. A medicinal tablet acording to claim 1 and substantially as set forth in any of the foregoing examples.

MARKS & CLERK,
Chartered Patent Agents,
Agents for the Applicant.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press.—1962.
Published by The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.

888038 COMPLETE SPECIFICATION
1 SHEET *This drawing is a reproduction of the Original on a reduced scale*

Fig.1.

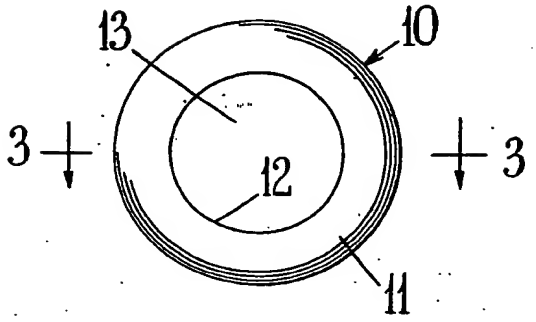

Fig.2.

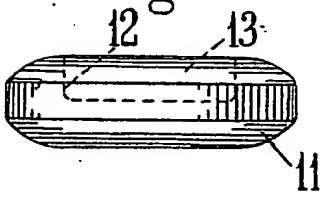

Fig.3.

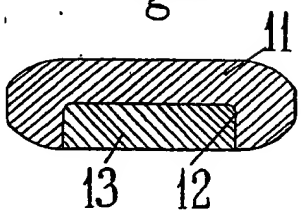

Fig.4.

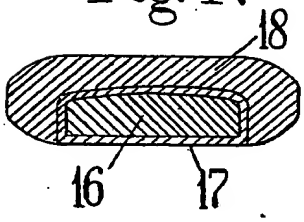

Fig.6.

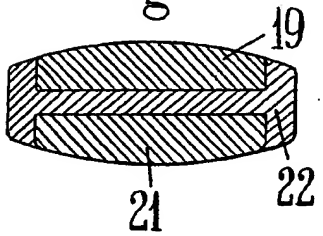

Fig.5.